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Before the First Cycle: Prognostic Nutritional Index as an Early Signal of Chemotherapy Intolerance in Solid Malignancies

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Abstract

Background: Nutritional impairment may reduce tolerance to systemic chemotherapy and contribute to treatment-related complications. This study evaluated the ability of pretreatment Prognostic Nutritional Index (PNI) to predict chemotherapy toxicity and treatment interruption in patients with solid malignancies.

Methods: This prospective observational study included 70 adults with solid malignancies receiving cytotoxic chemotherapy at DRIEMS Institute of Health Sciences, Odisha from May 2025 to January 2026. Baseline demographic, clinical, anthropometric, and laboratory parameters were recorded. PNI was calculated from serum albumin and absolute lymphocyte count, and patients were categorized as low PNI (<45) or preserved PNI (≥45). Patients were followed for three chemotherapy cycles. Grade ≥3 toxicity, neutropenia, treatment delay, dose reduction, hospitalization, and discontinuation were assessed.

Results: Low PNI was present in 29 (41.4%) patients. Grade ≥3 toxicity occurred more frequently in low-PNI patients than in those with preserved PNI (58.6% vs 24.4%; OR 4.39, 95% CI 1.57–12.26; p=0.004). Treatment delay (44.8% vs 14.6%; p=0.005), dose reduction (34.5% vs 12.2%; p=0.025), hospitalization (41.4% vs 14.6%; p=0.012), and grade ≥3 neutropenia (37.9% vs 14.6%; p=0.025) were also significantly higher.

Conclusion: Pretreatment PNI may provide a simple, inexpensive method for identifying patients at increased risk of chemotherapy intolerance and treatment disruption before initiation of systemic anticancer therapy.

Keywords: Chemotherapy toxicity; Nutritional status; Prognostic Nutritional Index; Solid malignancies; Treatment delay.

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Introduction

Malnutrition and systemic inflammation are common in solid malignancies and may adversely influence tolerance to anticancer therapy. Chemotherapy-related toxicities can lead to dose reduction, treatment delay, hospitalization, or premature discontinuation, compromising treatment intensity and outcomes. Nutritional assessment before systemic therapy provides an opportunity for early risk stratification. Recent evidence indicates that low body mass index and reduced Prognostic Nutritional Index (PNI), derived from serum albumin and lymphocyte count, are associated with poorer treatment completion and survival in anticancer therapy [1]. Nutritional deterioration has also been associated with unfavorable outcomes in advanced gastrointestinal cancers [2], while evidence supports the importance of nutritional management during cancer treatment [3]. Because PNI can be calculated from routine laboratory parameters, it may serve as a practical marker of chemotherapy tolerance. The present study aimed to evaluate whether pretreatment nutritional status, particularly PNI, predicts chemotherapy toxicity, treatment delay, dose reduction, and hospitalization in adults with solid malignancies.

Methods:

This prospective observational study was conducted in the Department of Medical Oncology, DRIEMS Institute of Health Sciences, Odisha, from May 2025 to January 2026. Adult patients aged ≥18 years with histologically or cytologically confirmed solid malignancies who were scheduled to initiate systemic cytotoxic chemotherapy were consecutively enrolled after obtaining written informed consent. Patients with hematological malignancies, active uncontrolled infection, severe hepatic or renal failure unrelated to malignancy, pre-existing severe malnutrition requiring parenteral nutritional support, concurrent chemoradiotherapy, or incomplete baseline investigations were excluded. Demographic and clinical information including age, sex, primary tumor site, disease stage, comorbidities, Eastern Cooperative Oncology Group (ECOG) performance status, treatment intent, chemotherapy regimen, height, weight, and body mass index (BMI) was recorded before the first chemotherapy cycle. Baseline laboratory investigations included hemoglobin, total leukocyte count, absolute lymphocyte count, platelet count, serum albumin, serum creatinine, and liver function tests. Pretreatment nutritional status was assessed using BMI and the Prognostic Nutritional Index (PNI). PNI was calculated using the formula: serum

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albumin (g/L) + 5 × absolute lymphocyte count (×10⁹/L). Patients with a PNI <45 were considered to have a low PNI, whereas those with a PNI ≥45 were categorized as having a preserved PNI. The study protocol was reviewed and approved by the Institutional Ethics Committee, and patient confidentiality was maintained throughout the study.

Patients were prospectively followed during the first three cycles of chemotherapy. At every cycle, clinical examination and routine hematological and biochemical investigations were performed, and treatment-related adverse events were documented. Chemotherapy toxicity was graded according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0. The primary outcome was the occurrence of clinically significant chemotherapy-related toxicity, defined as any grade ≥3 hematological or non-hematological adverse event during the observation period. Secondary outcomes included neutropenia, febrile neutropenia, anemia, thrombocytopenia, chemotherapy-related hospitalization, treatment delay, dose reduction, and premature treatment discontinuation. A chemotherapy delay was defined as postponement of a scheduled cycle by more than seven days because of toxicity or inadequate clinical recovery. Dose reduction was recorded when the planned chemotherapy dose was reduced because of treatment-related adverse effects. Data were entered into a structured database and analyzed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, while categorical variables were presented as frequencies and percentages. Associations between pretreatment PNI and chemotherapy outcomes were assessed using the chi-square/Fisher's exact test and appropriate tests for continuous variables. Multivariable logistic regression was performed to identify independent predictors of significant chemotherapy toxicity and treatment delay. A p value <0.05 was considered statistically significant.

Results:

A total of 70 patients with solid malignancies were included, of whom 29 (41.4%) had a low pretreatment PNI (<45) and 41 (58.6%) had a preserved PNI. The mean age of the study population was 56.2 ± 11.8 years, and 39 (55.7%) patients were male. Age, sex, and the proportion of patients with stage III–IV disease were comparable between the two PNI groups. Patients with low PNI had significantly lower BMI and serum albumin and more frequently had an ECOG performance status ≥2 (Table 1). During the first three chemotherapy cycles, 27 (38.6%) patients experienced grade ≥3 treatment-related toxicity. Significant toxicity occurred in 17/29 (58.6%) patients with low PNI compared with 10/41 (24.4%) patients with preserved PNI (OR 4.39, 95% CI 1.57–12.26; p=0.004). Treatment delay was significantly more common among patients with low PNI (44.8% vs 14.6%; OR 4.74, 95% CI 1.53–14.73; p=0.005). Low PNI was additionally associated with dose reduction, chemotherapy-related hospitalization, and grade ≥3 neutropenia. Febrile neutropenia showed a borderline association, whereas premature chemotherapy discontinuation did not differ significantly between groups (Table 2). Overall, impaired pretreatment nutritional status was associated with substantially poorer chemotherapy tolerance.

Discussion:

The present prospective study demonstrated a clinically important association between impaired pretreatment nutritional status and reduced chemotherapy tolerance among patients with solid malignancies. Of the 70 patients studied, 41.4% had a PNI <45, indicating that a substantial proportion entered systemic therapy with compromised nutritional and immunological reserves. Patients with low PNI had lower BMI and serum albumin and were more likely to have an ECOG performance status ≥2, suggesting that nutritional depletion occurred together with diminished functional reserve. Most importantly, grade ≥3 chemotherapy toxicity occurred in 58.6% of patients with low PNI compared with 24.4% among those with preserved PNI, corresponding to approximately four-fold higher odds of severe toxicity. These observations were consistent with Mota et al., who prospectively demonstrated that malnutrition assessed by the Patient-Generated Subjective Global Assessment predicted grade ≥3 toxicity and toxicity-related treatment modification during chemoradiotherapy [4]. Gascón-Ruiz et al. similarly showed that GLIM-defined malnutrition predicted complications among cancer outpatients [5]. PNI has particular clinical appeal because it incorporates serum albumin, reflecting nutritional and systemic inflammatory status, and peripheral lymphocyte count, which reflects immune competence. Chen et al. demonstrated the prognostic relevance of pretreatment PNI in breast cancer patients undergoing neoadjuvant chemotherapy and also identified relationships with hematological adverse effects [6]. Although these studies involved specific tumor populations, their observations support our finding that a simple baseline nutritional index may identify patients who are less physiologically equipped to tolerate cytotoxic treatment.

The association between low PNI and hematological toxicity was another important finding. Grade ≥3 neutropenia developed in 37.9% of low-PNI patients compared with 14.6% of patients with PNI ≥45, while febrile neutropenia was also numerically more frequent in the nutritionally compromised group. Liu et al. reported that patients with gastric cancer and low PNI experienced more severe hematological

toxic effects following adjuvant chemoradiotherapy, supporting the relationship between nutritional-immune impairment and bone-marrow toxicity [7]. More recently, Wei et al. evaluated patients with stage IV gastric cancer receiving first-line chemotherapy and found that low PNI, low Nutrition Risk Index and reduced skeletal muscle index were associated with early chemotherapy-induced myelosuppression [8]. Similar observations have extended beyond conventional chemotherapy alone. Hashino et al. assessed nutritional indices in patients receiving pembrolizumab combined with platinum-based chemotherapy for lung cancer and demonstrated clinically relevant relationships between nutritional indices, adverse events and treatment failure [9]. These findings are biologically plausible. Hypoalbuminemia may indicate inadequate protein reserves, inflammation or advanced disease, while lymphopenia may represent impaired immune function. Both components may coexist with reduced muscle mass, diminished drug-handling capacity and poorer physiological recovery following chemotherapy. Aberle et al. further showed that skeletal muscle parameters were independently associated with grade 3–4 toxicity in advanced pancreatic ductal adenocarcinoma receiving chemotherapy [10]. Therefore, the increased neutropenia observed in our low-PNI group likely represents part of a broader vulnerability phenotype rather than an isolated laboratory association.

The clinical consequences of this vulnerability were evident in treatment delivery. Chemotherapy delay exceeding seven days occurred in 44.8% of patients with low PNI compared with 14.6% of patients with preserved PNI, and dose reduction occurred in 34.5% versus 12.2%, respectively. Chemotherapy-related hospitalization was also substantially higher in the low-PNI group (41.4% vs 14.6%). These endpoints are particularly relevant because nutritional status becomes clinically meaningful when it influences the ability to deliver planned anticancer treatment rather than merely correlating with laboratory abnormalities. Hsueh et al. found that pretreatment albumin- and inflammation-based nutritional assessment was associated with chemotherapy completion and infection during neoadjuvant chemoradiotherapy for esophageal cancer [11]. Choi et al. reported that marked weight loss among patients receiving curative treatment for head and neck cancer was associated with substantially increased unplanned hospital admissions [12]. Fanetti et al. similarly demonstrated that PNI could predict treatment-related toxicity among patients with head and neck cancer undergoing definitive radiotherapy, particularly when chemotherapy was incorporated [13]. More recently, Zeynelgil et al. identified low PNI, low BMI and poor ECOG performance status as significant risk factors for failure to complete planned therapy in locally advanced head and neck cancer [1]. Collectively, these studies support the present results and suggest that pretreatment nutritional impairment contributes not only to adverse events but also to clinically consequential interruptions in systemic therapy. Recognition of low PNI before the first chemotherapy cycle may therefore provide an opportunity for closer monitoring, dietitian referral, correction of reversible deficiencies and individualized supportive care.

Several considerations should be applied while interpreting these findings. First, the study included only 70 patients from a single institution and encompassed different solid malignancies, stages and chemotherapy regimens; consequently, regimen-specific differences in toxicity may have contributed to the observed associations. Second, PNI was assessed primarily at baseline, whereas nutritional status may deteriorate dynamically during chemotherapy. Zhuang et al. demonstrated that serial nutritional assessment identified progressive nutritional deterioration and provided clinically meaningful prognostic information in patients with advanced gastrointestinal malignancies [2]. Future studies should therefore evaluate changes in PNI between chemotherapy cycles and determine whether improving nutritional status translates into better treatment tolerance. Third, although PNI is inexpensive and objectively calculated, no universally accepted cutoff exists across tumor types; the cutoff of 45 used in this study should therefore be externally validated. Furthermore, BMI alone cannot adequately characterize skeletal muscle depletion or sarcopenia, and future studies incorporating handgrip strength, CT-derived muscle measurements or standardized nutritional assessment tools may improve risk classification. Despite these limitations, the prospective design, systematic assessment of toxicity during the initial three chemotherapy cycles and evaluation of clinically relevant outcomes such as dose reduction, delay and hospitalization strengthen the study. The findings suggest that pretreatment PNI is a readily available marker that may complement ECOG performance status and conventional clinical assessment when identifying patients at increased risk of chemotherapy intolerance. Larger multicentric prospective studies are warranted to validate its predictive performance and determine whether PNI-directed nutritional and supportive interventions can reduce severe toxicity and improve continuity of chemotherapy.

Conclusion: Pretreatment nutritional impairment, reflected by a low Prognostic Nutritional Index, was strongly associated with poorer chemotherapy tolerance in patients with solid malignancies. Patients with PNI <45 experienced significantly higher rates of grade ≥3 toxicity, neutropenia,

treatment delay, dose reduction, and chemotherapy-related hospitalization compared with those having preserved PNI. These findings support the use of PNI as a simple, inexpensive, and readily available tool for identifying patients at increased risk of treatment-related complications before chemotherapy initiation. Incorporating PNI into routine pretreatment assessment may facilitate closer monitoring, timely nutritional intervention, and individualized supportive care, although larger multicentric studies are required for validation.

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Table 1: Baseline characteristics according to pretreatment Prognostic Nutritional Index

Variable	Total (n=70)	Low PNI <45 (n=29)	PNI ≥45 (n=41)	p value
Age, years, mean ± SD	56.2 ± 11.8	57.8 ± 11.5	55.1 ± 12.0	0.346
Male sex, n (%)	39 (55.7)	17 (58.6)	22 (53.7)	0.681
BMI, kg/m², mean ± SD	22.3 ± 3.4	20.7 ± 3.1	23.4 ± 3.2	<0.001
ECOG performance status ≥2, n (%)	20 (28.6)	12 (41.4)	8 (19.5)	0.046
Stage III–IV disease, n (%)	53 (75.7)	24 (82.8)	29 (70.7)	0.248
Serum albumin, g/dL, mean ± SD	3.61 ± 0.53	3.20 ± 0.40	3.90 ± 0.40	<0.001
PNI, mean ± SD	46.3 ± 5.7	40.9 ± 3.0	50.2 ± 3.6	—

PNI, Prognostic Nutritional Index; BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; SD, standard deviation. Continuous variables were compared using the independent-samples t-test and categorical variables using the chi-square test.

Table 2: Association between pretreatment PNI and chemotherapy-related outcomes

Outcome	Low PNI, n (%)	PNI ≥45, n (%)	Odds ratio (95% CI)	p value
Grade ≥3 toxicity	17 (58.6)	10 (24.4)	4.39 (1.57–12.26)	0.004
Treatment delay >7 days	13 (44.8)	6 (14.6)	4.74 (1.53–14.73)	0.005
Chemotherapy dose reduction	10 (34.5)	5 (12.2)	3.79 (1.13–12.69)	0.025
Chemotherapy-related hospitalization	12 (41.4)	6 (14.6)	4.12 (1.32–12.86)	0.012
Grade ≥3 neutropenia	11 (37.9)	6 (14.6)	3.56 (1.13–11.21)	0.025
Febrile neutropenia	7 (24.1)	3 (7.3)	4.03 (0.94–17.20)	0.048*
Premature treatment discontinuation	5 (17.2)	2 (4.9)	4.06 (0.73–22.62)	0.089

*PNI, Prognostic Nutritional Index; CI, confidence interval. The febrile-neutropenia estimate had a wide confidence interval and should therefore be interpreted cautiously despite the nominal p value.